Effects of manufacturing methods on the survival rate of ceramic and indirect composite restorations: A systematic review and meta-analysis

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Abstract: Objectives To evaluate the survival rate of ceramic and indirect composite inlays, onlays, and overlays manufactured according to different methods (CAD/CAM, pressable, and stratified). MEDLINE, EMBASE, and Cochrane Library databases were searched for published articles. Risk of bias, data extraction, subgroup analysis, meta-analysis, and GRADE was performed. Materials and methods Prospective, retrospective, or RCT studies, without restriction of language, from 1983 to 2019, with follow-up 5 years, reporting survival rates were screened independently by two reviewers in accordance with eligibility criteria. Results A total of 13 articles (12 for ceramic, one for indirect composite) met the inclusion criteria. No articles were included regarding crystalline ceramic. The estimated cumulative survival rate for CAD/CAM was 97% after 5 years and 89% after 10 years; for pressable was 95% after 5 years, and for stratified was 88% after 5 years and 93% after 10 years. Conclusions Regardless of the manufacturing method, vitreous ceramic inlays, onlays, and overlays showed high survival, providing evidence that these restorations are a safe treatment. Clinical relevance Vitreous ceramic inlays, onlays, and overlays showed high survival, regardless of the manufacturing method, providing evidence that these restorations are a safe treatment.

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Effects of manufacturing methods on the survival rate of ceramic and indirect composite restorations: A systematic review and meta-analysis

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KEY WORDS: Ceramics; Dental porcelain; Composite resin; Inlays; Systematic review.

ABSTRACT

Objectives: To evaluate the survival rate of ceramic and indirect composite inlays, onlays, and overlays manufactured according to different methods (CAD/CAM, pressable and stratified). MEDLINE, EMBASE and Cochrane Library databases were searched for published articles. Risk of bias, data extraction, subgroup analysis, meta-analysis, and GRADE was performed.

Materials and Methods: Prospective, retrospective, or RCT studies, without restriction of language, from 1983 to 2019, with follow-up ≥ 5 years, reporting survival rates were screened independently by two reviewers in accordance with eligibility criteria.

Results: A total of 13 articles (12 for ceramic, 1 for indirect composite) met the inclusion criteria. No articles were included regarding crystalline ceramic. The estimated cumulative survival rate for CAD/CAM was 97% after 5 years and 89% after 10 years; for pressable was 95% after 5 years, and for stratified was 88% after 5 years and 93% after 10 years.

Conclusions: Regardless of the manufacturing method, vitrous ceramic inlays, onlays, and overlays showed high survival, providing evidence that these restorations are a safe treatment.

Clinical Relevance: Vitrous ceramic inlays, onlays, and overlays showed high survival, regardless of the manufacturing method, providing evidence that these restorations are a safe treatment.

Keywords: Ceramics, Composite resin, Inlays, Systematic review, Survival analysis.

1.INTRODUCTION

Ceramics and composites have characteristics with regard to structure and manufacturing methods, that associated with the luting agents, and intraoral conditions are important factors attributed to longevity of inlay, onlay and overlay restorations,[1,2-10,11,12] being clinicians responsible for the decision-making process. However, this choice is conducted based on criteria such as strength, translucency/opacity degree, preference of dental laboratory technician, and advertising claims.[13] On the other hand, manufacturing methods directly influences on several of these criteria, being strength the most important factor for the survival rate, once fractures were the most frequent cause of failure.[2]

Indirect esthetic materials may be clustered into two groups: ceramics (crystalline or vitreous ceramics (feldspathic porcelain and glass ceramic)), and composites. [4,8-10,12-14] Feldsphatic porcelain may be found in powder (stratification) or block (CAD/CAM) forms. Glass ceramics (fluorapatite, leucite or lithium-disilicate) are available in the form of powder (stratification), ingots (heat-pressable), or blocks (CAD/CAM). Alumina or zirconia crystalline ceramics are available in powder form (stratification and densely sintered) or blocks (CAD/CAM). Indirect composites restorations are fabricated by means of chemical, heat, light cure, or from blocks (CAD/CAM).[2,8-12]

CAD/CAM technology is a great 3D innovation used to machine pre-fabricated blocks to build a substructure stratified with porcelains or glass-ceramics, or monolithic restorations characterized by external stains.[10,11,13-15]

Sequential layers stratification with different high- or low-fusing ceramics, translucence/opacity degrees, and fluorescent-, opalescent-, and translucent-like effects, make possible to fabricate esthetic ceramic restorations with an excellent naturalness. However, these restorations are very fragile before cementation.[10,14]

Pressable ceramics are manufactured from monochromatic glass-ceramic ingots, which are heated to allow material to flow under pressure into a mold formed by using lost-wax technique; and would have to be superficially stained only, or stratified. This technique shows better adaptation and higher strength.[10,14]

Indirect composite restorations can be obtained from a temperature, humidity, time, and light-controlled environment, resulting in a well-cured restoration with improved mechanical properties.[16] Pre-fabricated blocks, with relatively pore free structure, have high-quality polymers, and better properties of polishability, reduced pigmentation and increased strength.[12,13]

Restorations survival rates fabricated with different materials are still a frequent topic in primary studies.[11-35] In dental prosthesis, there is still a lack of randomized clinical studies. Consequently, in previous systematic reviews, [6,7,36-38] where only RCTs were included, elegibility criteria became very strict. This could be the reason why authors were unable to gather strong evidence about that matter, especially in follow ups over 5 years. Survival rate of inlay and onlay CAD/CAM restorations was 92.9% after 5 years, analyzing a pool of single-tooth restorations.[39] With the foregoing considerations in mind, this study sought RCTs, both prospective and retrospective studies, in order to evaluate trends in ceramic and composite inlays, onlays and overlays that needed to be investigated.

The influence of different manufacturing methods on the esthetic inlays, onlays, and overlays is a very important clinical information for clinicians to support their decisions, since manufacturing methods are still an unknown variable for the restoration success. Based on previous systematic reviews,[2,3,6,7,9,36-39] there is still a literature gap, justifying the conduction of a systematic review on this scope.

Thus, the aim of this systematic review was to evaluate the survival rate of indirect composite and ceramic inlays, onlays and overlays, following different manufacturing methods.

METHODS

Search strategy and eligibility of articles

Advanced searches were performed in the MEDLINE/Pubmed, EMBASE and Cochrane Central Register of Controlled Trials (until January 09, 2019) databases. Studies related to ceramic and indirect composite inlay, onlay and overlay restorations were included. The inclusion period was 1983 to 2017 without language restriction. Two articles that standardized the resin adhesive procedures for ceramics with the use of hydrofluoric acid and silane defined 1983 as the beginning year for this search.[40,41] References of all included articles were checked manually. PRISMA-P guidelines [42] were strictly adhered to this review.

Initially, the PICOS question (Population, Intervention, Comparison; Outcomes and Study design) was defined as follows: P= patients who received indirect composite or ceramic inlays, onlays, and overlays; I= inlays, onlays, and overlays made of ceramic or indirect composite; C= not applicable in this study; O= survival rate; S= randomized controlled clinical trials (RCT) and clinical follow-up studies.

The final strategy chosen for research in MEDLINE was: ((((((inlay*) OR onlay*) OR overlay*) OR coverage)) AND ((((((porcelain*) OR ceram*) OR resin) OR ceromer) OR CAD-CAM) OR CEREC)) AND ((((((((((clinical evaluation) OR clinical trial[MeSH Terms]) OR longevity) OR success) OR failure) OR survival rate[MeSH Terms]) OR clinical performance) OR follow up study[MeSH Terms]) OR clinical study) OR comparative study)). For the research in EMBASE, the following final search was used: 'ceramics'/exp OR 'porcelain' OR 'porcelain tooth'/exp OR 'resin'/exp OR 'ceromer' AND ('dental inlay'/exp OR 'ïnlay' OR 'onlay' OR 'overlay') AND ('clinical trial'/exp OR 'clinical study'/exp OR 'intervention study'/exp OR 'prospective study'/exp OR 'retrospective study'/exp OR 'follow up'/exp) NOT [medline]/lim AND [embase/lim AND [1983-2014]/py. The search strategy in Cochrane Central Register of Controlled Trials was as follows: ((inlay or onlay or overlay) and (ceramic or resin) and (dental or tooth or teeth) and (clinical and trial or clinical)).

Study Selection and Eligibility Criteria

Studies were selected by title and abstract according to the inclusion criteria: 1) studies related to ceramic or indirect composite inlays, onlays and overlays; and 2) categorized as prospective/retrospective studies or randomized controlled trials (RCTs) conducted in humans with availability of clinical follow-up data. Articles without abstracts or articles with an abstract with insufficient descriptions to enable decision were included for full text evaluation.

Eligibility was determined after full text assessment and rejection of inappropriate studies according to the exclusion criteria: 1) articles without description of the procedure, or when uncommon preparations had been performed (such as bridge

abutments, splinting, uncommon bonding procedures, occlusal coverage of posterior teeth without preparation, implant abutments); 2) case reports; 3) literature or systematic reviews, protocols, interviews, and in vitro studies; 4) studies conducted in isolated groups (bruxism, hypoplasias, others); 5) studies with the same sample (the most recent and/or with most complete data was considered); 6) studies without survival analysis or with incomplete data for proposed analyses; 7) studies with drop-out rate higher than 30%; 8) studies with follow-up shorter than 5 years and 9) studies describing manufacturing methods that are no longer used or with incomplete data.

Data collection process

All the stages of the literature review, data collection, and characteristics of the studies were performed by two independent, calibrated examiners (FBWRS, SM), and Kappa test was calculated, requiring a minimum agreement of 0.80, in order to obtain a higher degree of agreement in the evaluation of studies. Discrepancies were resolved by consensus and a third examiner (TG) was consulted.

Assessment of risk of bias

Two calibrated examiners (FBWRS and SM) assessed the included studies risk of bias. In this systematic review, 12 observational studies were included after full-text reading, therefore assessment tools such as the Newcastle-Ottawa Scale (NOS) adapted by Chambrone et al. (2015) are recommended. [43] The following criteria were assessed: The questions were as follows: a) selection of study groups: sample size calculation; representativeness of the patients treated with each

method, detailed description of the steps following for all required procedures, training/calibration of the operators and assessors of outcomes and appropriate protocol of data collection; b) comparability: comparability of patients on the basis of the study design or analysis and management of potential confounders; c) outcomes: evaluation of results, assessment of accuracy outcomes and adequacy of follow-up of the patients and d) statistical analysis: appropriateness/ validity of statistical analysis and unit of analysis reported in the statistical model. A maximum of 13 stars could receive each included study. Studies with 10 - 13 points were arbitrarily considered as being of high, with 7-9 points of medium and with < 7 points as being of low methodological quality.

The recommendations for systematic reviews of interventions of the Cochrane collaboration[44] were performed to evaluate a risk of bias of the only one RCT included. The following criteria were assessed: a) andom sequence generation; b) allocation concealment (both accounting for selection bias); c) blinding of participants and personnel (performance bias); d) blinding of outcome assessment (detection bias); e) incomplete outcome data (attrition bias); f) selective reporting (reporting bias) and g) other possible causes of bias.

The risk of bias in the included studies was categorized according to the following criteria: 1) low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met; 2) unclear risk of bias (plausible bias that raises some doubt about the results) if one or more criteria were partly met and 3) high risk of bias (plausible bias that seriously weakens confidence in the results) if one or more of the criteria were not met.

Evaluation of quality of evidence—GRADE approach

GRADE criteria were used to assess the effects of other variables rather than risk of bias (such as inconsistency, heterogeneity, indirect evidence, and imprecision) on the confidence in overall results at outcome level by two calibrated examiners (FBWRS and SM). Confidence is scored as very low, low, moderate and high, and the reason for downgrading was reported.

Measures and statistical analysis

Descriptive statistics and meta-analysis were performed for estimated survival rates analyses. A Cochran Q test was performed ($p < 0.001$/CI 95%) to evaluate the presence of heterogeneity among studies and the presence and extent of heterogeneity was measured using an inconsistency test ($I^2 > 50\%$), since there is a small number of included studies, both tests present low statistical power, and thus results should be interpreted with caution.[44] The inverse variance method was used, with the estimator of DerSimonian-Laird for the I^2. Data were transformed and the individual CI of studies was calculated by the Clopper-Pearson method (Software program R 3.1.0, R Core Team, 2014) with the aid of the Meta package.[45]

Meta-analysis with survival rates was performed including studies evaluating survival rates for each manufacturing method individually (CAD/CAM, pressable and stratified). When studies did not present variance (or standard deviation), it was calculated, analyzing the number of failures and censorship during the follow-up time. Data were collected from texts or calculated using the Kaplan-Meier graphs[19-21,23,25-29] or life tables[22,24] for those articles where estimate of survival in the specific periods

(5 and 10 years) was not explicit. Greenwood formula[46] was used to calculate variance, assuming that censorships occurred uniformly over time, together with failures.

RESULTS

Study selection

Search strategies identified 1615 studies. After titles and abstracts evaluation, and duplicates elimination, 296 studies were selected, from which 283 were further excluded after full text reading (Figure 1). Finally, 13 articles were considered for quantitative (Figure 3- 5) and risk of bias analyses (Figure 2), being 12 articles for ceramic restorations and 1 article for indirect composite restorations. The level of agreement between examiners for the inclusion stage and for the eligibility stage of the review was 0.9 and 0.8 (Cohen´s kappa), respectively.

Assessment of risk of bias

Details of the assessment of the risk of bias for the observational studies (12) and RCT (1) were displayed in Figure 2A and Figure 2B, respectively. Therefore, all of 13 studies included were arbitrarily considered as being of high methodological quality.

Evaluation of quality of evidence—GRADE approach

The evaluation of the quality of evidence is displayed in Table 1. Considering the overall assessment of the quality of evidence were scored as moderate, because

this systematic review included only one RCT with slight limitations and 12 well-delineated observational studies with consistent findings. Despite the high quality of evidence in 4 items, the indirect evidence obtained moderate quality, being the main reason for downgrading the confidence of the analysis. When studies did not directly compare the interventions (head-to-head), effect estimates are presented based on indirect comparisons, providing compelling reasons why the indirect estimate is likely to be biased.

Characteristics of studies

Publication year of included studies ranged from 1987 to 2019. Information and characteristics of each study are provided in Table 2. From studies including same sample,[31,34] the most recent study was considered. However, there was one exception[35] where the oldest study was selected,[19] since the most recent one presented incongruous data with respect to the distribution number of men and women, number of failures per patient, and number of secondary carious lesions. Another exception, the most recent paper was excluded by the drop-out rate higher than 30%[50].

Measures and statistical analysis

Indirect composite

One study of indirect composite inlays, onlays, and overlays[12] could be identified in the data collection process; hence meta-analysis could not be performed for this material. Authors concluded that in a 5-year period, resin cuspal coverage of endodontic treated teeth had a success rate of 96% and the tooth survival rate was

100%. Thordrup et al. (2006) [5] evaluated the survival rate of ceramics and composites, fulfilling various inclusion criteria, but they did not present the number of patients per material.

Ceramics

Subgroup analysis and meta-analysis for inlays, onlays, and overlays.

Meta-analysis was performed by separating CAD/CAM, pressable, and stratified manufacturing methods, including studies that evaluated survival rates for each technique, respectively. Twelve studies were retained for quantitative analysis: 5 with CAD/CAM, 3 with pressable, and 4 with stratified method. In the CAD/CAM group, glass ceramics and feldspathic porcelains were included; in the pressable group, only glass ceramics; and in the stratified group, only feldspathic porcelains. Analyses of survival in the subgroups were then performed for each manufacture method.

For the CAD/CAM group, with a clinical follow-up time of 5 years (N = 3746), the cumulative survival rate was 97% (95%CI: 97% to 98%; $I^2 = 0\%$; p = 0.41) (Figure 3A). For the clinical follow-up time of 10 years (N = 1259), the survival rate was 89% (95% CI: 87% to 91%; $I^2 = 0\%$; p = 0.99) (Figure 3B). For the pressable group, with a clinical follow-up time of 5 years (N = 909), the cumulative survival rate was 95% (95%CI: 93% to 96%; $I^2 = 0\%$; p = 0.97) (Fig 4). Only one study[27] presented a clinical follow-up time of 10 years. For the stratified group, with a clinical follow-up time of 5 years (N = 413), the cumulative survival rate was 88% (95%CI: 71% to 96%, $I^2 =$

91%; p < 0.01) (Figure 5A). For the clinical follow-up time of 10 years (N = 290), the survival rate was 93% (95% CI: 67% to 99%; I^2 = 92.4%; p = 0.0003) (Figure 5B).

DISCUSSION

No previous systematic reviews have analyzed the influence of different manufacturing methods on the survival rates of ceramics and indirect composite inlays, onlays and overlays. In this study, there was no influence for this outcome when different manufacturing methods were considered. Focusing in this scope, one systematic review[3] assessed the clinical outcomes only for CAD/CAM ceramic inlays. However, authors were unable to perform a meta-analysis. In other systematic review,[39] a survival rate of 92.9% after 5 years only for inlay and onlay CAD/CAM restorations was found, analyzing a pool of single-tooth restorations.

Regardless of manufacturing methods, inumerous previous systematic reviews were unable to perform a meta-analysis concerning survival rates of indirect composite or ceramic inlays, onlays, and overlays.[3,6,36,37]. A systematic review conducted by Fron Chabouis et al. [7] comparing indirect composite and ceramic inlays, onlays, and overlays, concluded there was very limited evidence of a better performance of ceramics in comparison to composite materials for inlays in the short term (only 2 RCTs were included in the analysis). Pol and Kalk,[6] in the Hayashi et al. [36] systematic review update, concluded that the strict inclusion criteria predetermined a small sample, turning it infeasible to perform a meta-analysis. Recommendations were made for the establishment of less strict criteria allowing the inclusion of more

references. Grivas et al. [37] affirmed there is insufficient evidence to determine differences in longevity between direct and indirect composite inlays on the one side and ceramic and gold inlays on the other.

In our previous systematic review [2], estimated survival rates for inlays, onlays, and overlays manufactured by glass-ceramics and feldspathic porcelain of 92% at 5 yrs. and 91% at 10 yrs., were found. Fractures were the most frequent cause of failure. On the basis of this and others systematic reviews on this subject, a lack of clinical evidence about the best fabrication technique for indirect composite or ceramic inlays, onlays and overlays, was found.

Before the conduction of time-consuming and costly clinical studies, preclinical in vitro studies should be considered to evaluate prothesis durability.[1] In vitro articles have also studied existing differences such as fracture resistance of pressable vs. CAD/CAM ceramics onlays. [8] According to this study[8] both onlay fabrication system and adhesive cements could be viable treatment options. Another point to be discussed is marginal fit. One study affirmed press fabrication resulted in a superior internal fit of onlays when compared to CAD/CAM technique, but the mean values of marginal gaps in the investigated onlays, before and after luting, and fatigue, were clinically acceptable. Marginal fit was not affected by the investigated heat-press versus CAD/CAM fabrication technique.[49] Other study[50] evaluated the effect of different manufacturing methods of resin and ceramic inlays on marginal and internal adaptation, adjustment time, and proximal contacts. Groups were LaRe—digital impression with a Lava C.O.S. scanner/milling of Lava Ultimate block (composite resin); CeRe—digital impression with a Cerec 3D Bluecam scanner/milling of Lava

Ultimate block in Cerec; CeDis—digital impression with a Cerec 3D Bluecam scanner/milling of IPS e.max CAD block (lithium disilicate) in Cerec; and PresDis- impression/pressed (IPS e.max Press- lithium disilicate). Analyses for marginal fit showed many differences at the cervical edge, but all groups presented similar adaptation at the occlusal one and similar internal fit at the pulpal wall. The lowest proximal contact was seen in the CeRe group.

Therefore, after looking for *in vitro* studies, systematic reviews and clinical trials about the influence of manufacturing methods on the survival rate of ceramic and composite inlays, onlays, and overlays, the need of information regarding the clinical performance of such restorations in the oral environment, over time, was rose. Thus, this systematic review, based only on clinical trials, both prospective and retrospective, was conducted to clarify this question.

Accordingly, retrospective studies were also included, and some of the advantages of including this type of studies are the large number of patients, and the wide variety of materials and operators. Furthermore, these studies were often able to follow the evolution of techniques and materials, continually updating sample size and frequently contemporary with new clinical realities. Thus, the inclusion of retrospective studies was important to explain current trends. In contrast, clinical trials were developed in small and select patient groups, generally with an interval of less than 5 years; however, with a highly strict methodology.[18]

The present study included data from only two ceramics (feldspathic porcelain and glass ceramics) and from three manufacturing methods (CAD/CAM, pressable,

and stratified). Therefore, it was not possible to accomplish a meta-analysis concerning manufacturing methods of indirect composite or crystalline ceramic inlays, onlays, and overlays, since only one and none study were selected, respectively.

In order to assist the evaluation of possible sources of heterogeneity, visual inspection was performed on each analyzed subgroup (Figure 3-5). Only the stratified group presented a high heterogeneity (Figure 5) and for all the others subgroups was 0%. In reality, a high level of heterogeneity was expected, because clinical articles generally present many methodological and clinical variations. The random effect model was used for the analyses when I^2 was higher than 50%.[45]

Well defined success and survival criteria are of great importance to ensure authors are not too strict or too flexible when classifying failures. The lack of standardization over the concepts difficulties a better understanding of outcome results. Differences between authors in relation to what was considered as failures may have changed the mean failure of a given outcome, e.g chipping and fracture concepts were often merged, and sometimes not even considered as failures if a burnish or composite repair was agreed with the patient. Survival and success concepts must be very evident and, perhaps, identification of both data on articles avoid so many divergency. Survival of teeth or restoration is also an important difference. This lack of concepts standardization seems to be a strong possibility for heterogeneity cause.

Presentation of both rates could be helpful to future meta-analyses. In the present study, pooled estimated survival rates at the follow-up times of 5 and 10 years were 97% and 89%, respectively, for the CAD/CAM method. After 5 years, survival rate for pressable glass ceramics was 95%. For the stratified group, survival rates at the follow up times of 5 and 10 years were 88% and 93%, respectively. Only

the stratified group presented a lower survival rate at the 5-year follow-up than after 10 years. This was due to the inclusion of the Smales and Etemadi[24] study, that presented lower survival rates than those found in other studies. Authors concluded that including bruxist patients led to a higher number of fractures, but this statement should be interpreted with caution as currently there is no consistent evidence to support an association between bruxist patients and increased number of fractures in regards to ceramic restorations.

From a clinical point of view, CAD/CAM, pressable, and stratified manufacture present no significant differences in survival rates, regardless of time, ceramic material, or laboratory methods. This could be explained by the strong bond between ceramics and dental structure when a protocol of acid etching and silanization of vitreous ceramic is used. In this manner, the strength of all porcelains is increased, and clinically behave in a similar manner.[8,14] Another factor that may explain the similar behaviour of these materials is the fact that many glass ceramic copings are stratified from vitreous ceramics in powder/liquid form. Generally, fracture and chipping are two of the main causes of failures, occurring in the covering ceramics, which may be feldspathic porcelains or glass ceramics in powder form. Observation that covering ceramics are less resistant than ceramic coping has been shown in several studies.[4,6,9,48] Indeed, the core-veneer bond strength is one of the weakest links of layered all-ceramic restorations, and it has a significant role on their survival.[3,40]

Positive aspects of this study include improvements in both methodological delineation and description of data. Another significant improvement is the reliance on recent clinical studies (only studies from 1997 - 2017 were included), which tend to demonstrate more robust statistics. In the eligibility stage, from the 283 accessed

articles in full text, 128 were excluded as they did not present survival rates or lacked complete data for analysis. Based on the present review and on several previous systematic ones about inlay, onlay, and overlay restorations, there is a gap in clinical evidence concerning the best fabrication technique for indirect composite or crystalline ceramic restorations, pressable ceramics after 5 years, and ceramics (milled, stratified, or pressable) after 10 years.

This review had, a priori, its protocol based on PRISMA-P and is part of a broad systematic review, which was initially published with endings targeting the different types of preparation and restorative materials [2], and in this paper the outcome was clustered according to manufacturing methods, thus, this systematic review was not registered in the PROSPERO at the time. However, the authors emphasize the absence of bias reporting. The other limitation is that a small number of included studies, Cochran Q and I-squared tests present low statistical power, and thus results should be interpreted with caution.

Restorative treatments should be explored from a broader perspective than just the longevity of treatment. Dental patient-reported outcomes measures (dPROMs) are importantes end points,[52, 53] since they can clarify relevant questions about the management of dental diseases, as well as act as a tiebreaker to choose a treatment.[54] Being a recent trend in dentistry, these outcomes are largely unexplored and quality of publications in this area needs to be improved.[53-55] Thus, health professionals should seek alternative treatments that obtain high levels of survival, but which provide minimal intervention, with lower cost, operative time, and patient perceived impact.[53, 55, 56]

Risk of bias analysis in conjunction with studies characteristics may help to understand differences among included articles. Questions about the risk of bias also serve as a good guide for the planning of future clinical studies, as they present important concepts necessary for a valid study. Quality of the evidence (GRADE) was considered moderate, since the survival rate was considered a critical outcome for decision making, and this one remained high, regardless of time, can be inferred in a more pragmatic evaluation of the balance between risks and benefits points to a safe clinical recommendation.

Additional well-designed randomized clinical studies comparing laboratory manufacturing methods and materials, with detailed samples, description of censorship in survival graphs, drop outs, description of failures classified as acceptable or unacceptable, better standardization of the evaluation criteria, and separation of the survival and success rate should be conducted, as well as, that consider the points that affect the risk of bias of included studies and, specifically, decision making supported by high-level of informed and trustworthy evidence.

CONCLUSIONS

Regardless of the manufacturing methods, vitreous ceramic inlays, onlays, and overlays showed high survival, providing evidence that these restorations are a safe treatment, but no conclusive evidence is available about indirect composite or crystalline ceramic inlays, onlays and overlays. Based on risk of bias and quality of evidence, the current evidence level for this clinical approach is low and high-moderate, respectively.

LEGENDS

Table 1 - Evaluation of quality of evidence—GRADE approach

Quality assessment							Summary of Findings				Relevance
							Number of patients			Quality (GRADE)	
Study	Desing	Limitations	Inconsistency	Indirectness	Imprecision	Other Factors	Pressed	Stratified	CAD/CAM		
13	Observational/ RCT	No serious limitations (H- high quality)	No serious Inconsistencys (H- high quality)	(M- Moderate quality)	No serious imprecision(H- high quality)	None	909	413	3746	HHMH HIGH-MODERATE	Critical

- Total of 13 articles (12 articles for ceramic and 1 article for indirect composite).
- Study Desing - 12 Observational Studys and 1 RCT.
- Based on risk of bias, all studies were classified as high methodological quality.
- No head to head comparison.
- The amplitude of IC (95%) is relatively low in most studies, and the intervention has no adverse effects, with good acceptability and moderate cost. Also, the small number of failures allows the survival rate to remain high at 5y and 10y.

Table 2 - Study characteristics of 12 articles of ceramic and 1 article of indirect resin (*) included.

Author	Year	Material/ Method	Idiom	Country	Inclusion period	Evaluation criteria	Follow up period	Setting/ operator	Age range (y)	N patients	Drop out (%)	Study	N restoration	Survival (%)
Dias et al.*	2016	Indirect resin (Photo + Thermo)	English	Portugal	2009-2012	Ns	5 y	Acad./ 1op	Ns	150	0	PC	150	96
Nejatidan et al.	2015	Glass ceramic (CAD/CAM)	English	Isfahan	03/2009-09/2009	CDA	5 y	Private/1 op	18-70	109/103	5.50	PC	159/153	95.5
Frankenberger et al.	2008	Glass ceramic (Pressable)	English	Germany	Ns	Modified USPHS	12y	Acad./6 op	20-57	34/26	23.5	PC	96/58	86
Krämer et al.	2008	Glass ceramic (Pressable)	English	Germany	Ns	Modified USPHS	8y	Acad./6 op	24-54	31/23	25.8	PC	94/68	90
Otto & Schneider	2008	Feldspathic porcelain. (CAD/CAM)	English	Switzerland	1989-1991	Modified USPHS	17 (16 y 11mo)	Private/1 op	17-75	108/89	17.59	RC	200/187	88.7
Reiss	2006	Feldspathic porcelain+ Glass ceramic (CAD/CAM)	English	Germany	1987-1990	CDA/Rygge	18.3y	Private/ ns op	12-70	299	0	RC	1011	89
Schulte et al.	2005	Glass ceramic (Pressable)	English	Germany	1993-2002	Ns	9.6y	Acad./244 op	17-64	434/390	10.13	RC	810/783	90

Smales & Etemadi	2004	Feldspathic porcelain (Stratified)	English	Australia	1988-1995	Ns	6y	Private/ 2 op	15->50	50	0	RC	78	60.5 +/- 6.3
Sjögren et al.	2004	Feldspathic porcelain (CAD/CAM)	English	Sweden	Ns	Modified USPHS	10y	Acad./3 op	26-73	27/25	7.4	RCT	66/61	89
Schulz et al.	2003	Feldspathic porcelain (Stratified)	English	Sweden	1988-1997	CDA/Rygge	9y	Private/1 op	28-79	52/51	1.92	RC	109/107	84
Posselt & Kerschbaum	2003	Ceramics (ns) (CAD/CAM)	English	Germany	1990-1999	Ns	9.1y	Private/ns op	17-75	794	Ns	RC	2328	95,5
Hayashi et al.	2000	Indirect resin (Photo + Thermo)	English	Japan	1990-1991	Modified USPHS	8y	Univ./ ns op	ns	29/25	13.79	RC	49/45	80
Fuzzi & Rappelli	1998	Glass ceramic (CAD/CAM)	English	Italy	1986-1996	Modified USPHS	10y	Private/1 op	21-58	67	0	RC	183	97

Legend: Ns= not specified; y= year; mo= months; N= Number; ns op= not specified operator; RC= Retrospective cohort; PC= Prospective cohort; Acad.=University or institute.

FIGURE LEGENDS

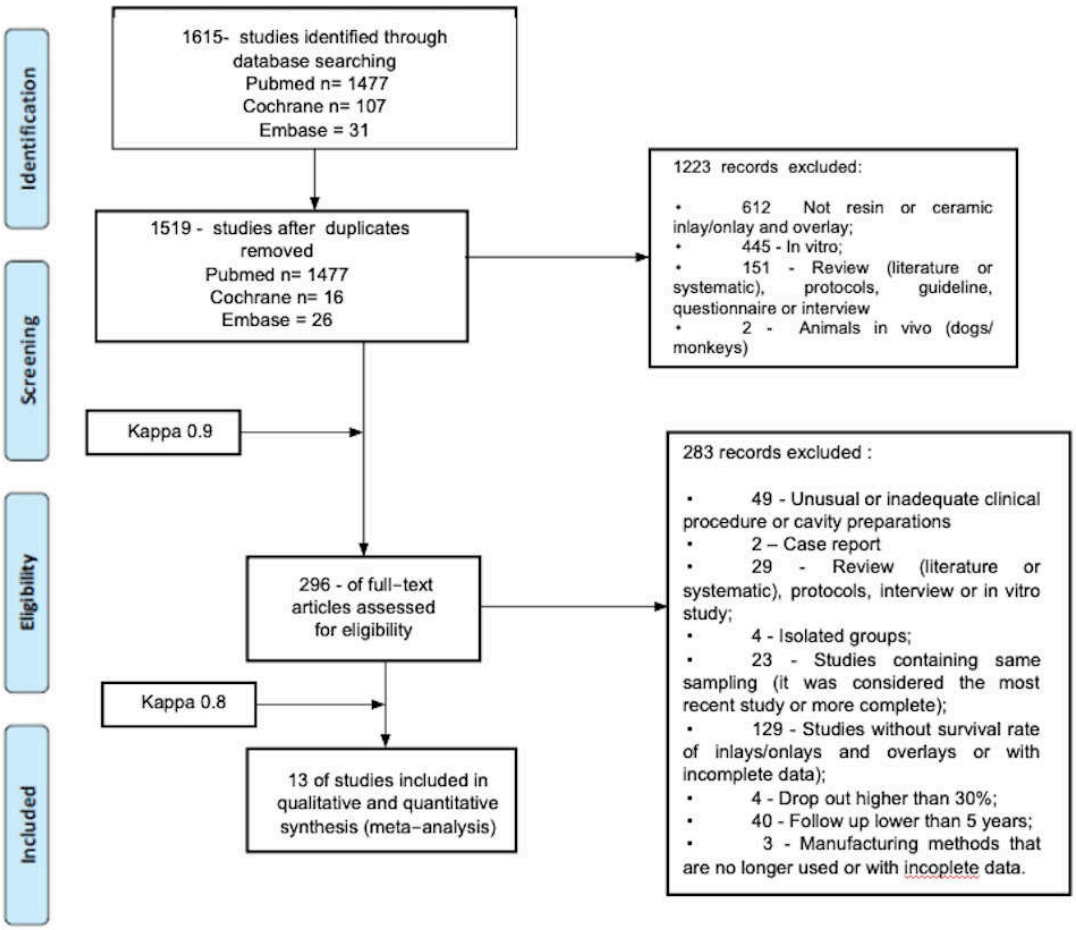
FIGURE 1 Flow diagram with the information through the phases of study selection based on PRISMA (Moher et al. 2009) [42]

FIGURE 2 A: Risk of bias of included observational studies. **B:** Risk of bias of RCT included

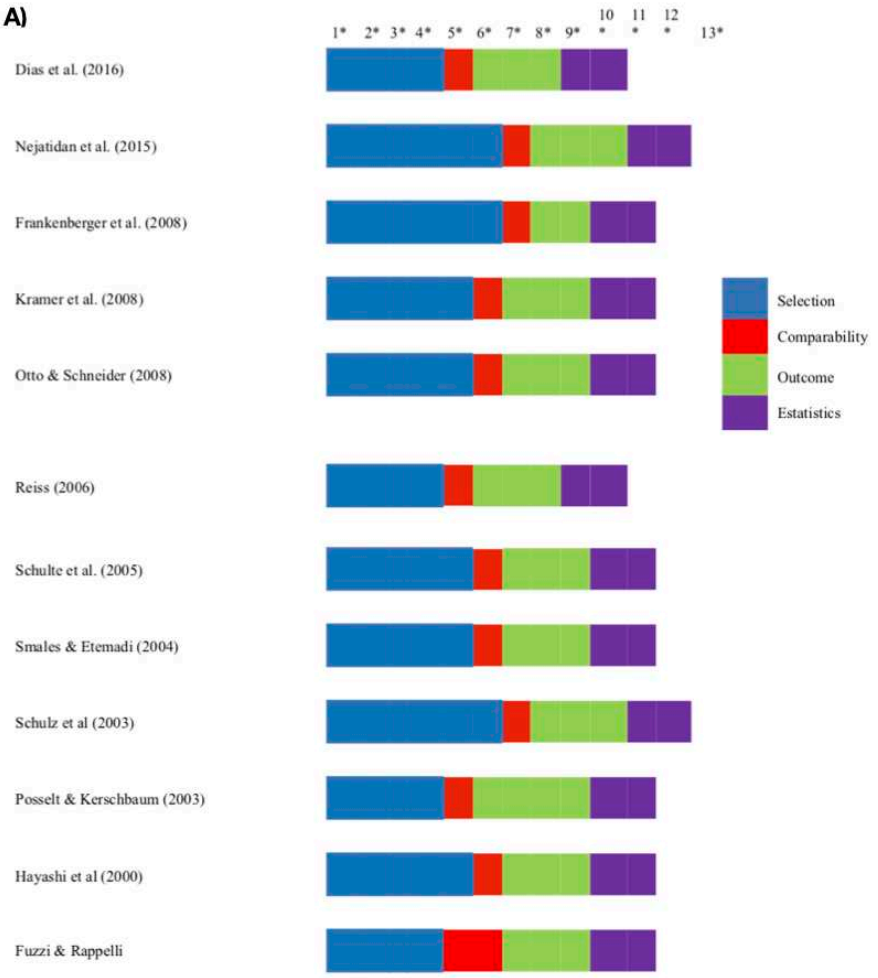
FIGURE 3 A: Forest plot of CAD/CAM group (estimated cumulative overall survival rate for 5 years – 5 included studies). **B:** Forest plot of CAD/CAM group (estimated cumulative overall survival rate for 10 years - 3 included studies)

FIGURE 4 Forest plot of pressable group (estimated cumulative overall survival rate for 5 years - 3 included studies)

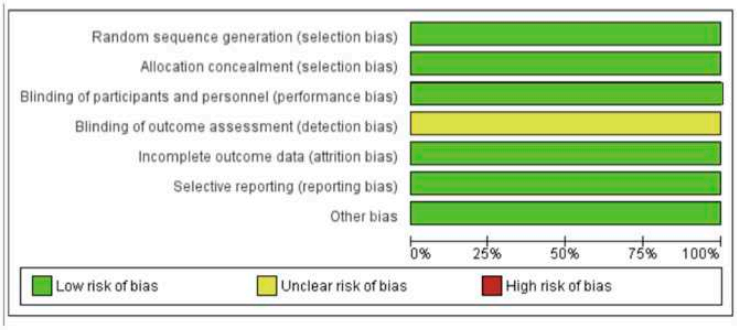
FIGURE 5 A: Forest plot of stratified group (estimated cumulative overall survival rate for 5 years - 4 included studies). **B:** Forest plot of stratified group (estimated cumulative overall survival rate for 10 years - 2 included studies)

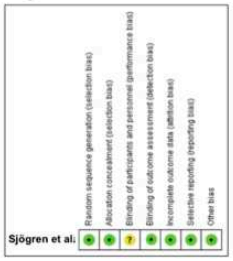

Identification
Screening
Eligibility
Included
1615- studies identified through database searching
Pubmed n= 1477
Cochrane n= 107
Embase = 31
1519 - studies after duplicates removed
Pubmed n= 1477
Cochrane n= 16
Embase = 26
1223 records excluded:
• 612 Not resin or ceramic inlay/onlay and overlay;
• 445 - In vitro;
• 151 - Review (literature or systematic), protocols, guideline, questionnaire or interview
• 2 - Animals in vivo (dogs/ monkeys)
Kappa 0.9
296 - of full-text articles assessed for eligibility
283 records excluded :
• 49 - Unusual or inadequate clinical procedure or cavity preparations
• 2 – Case report
• 29 - Review (literature or systematic), protocols, interview or in vitro study;
• 4 - Isolated groups;
• 23 - Studies containing same sampling (it was considered the most recent study or more complete);
• 129 - Studies without survival rate of inlays/onlays and overlays or with incomplete data);
• 4 - Drop out higher than 30%;
• 40 - Follow up lower than 5 years;
• 3 - Manufacturing methods that are no longer used or with incoplete data.
Kappa 0.8
13 of studies included in qualitative and quantitative synthesis (meta-analysis)

A)

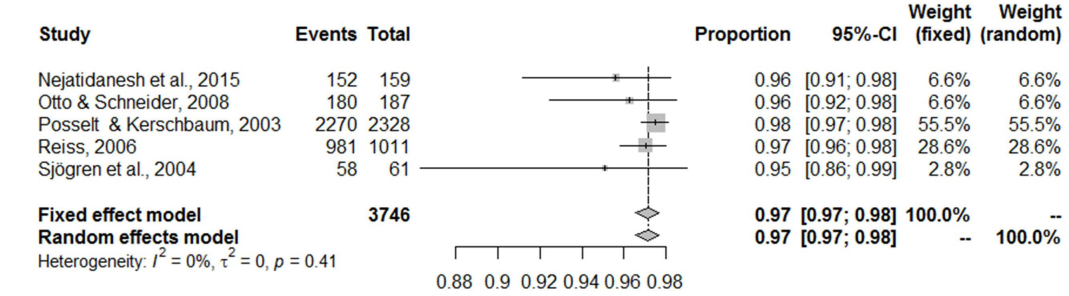

1* 2* 3* 4* 5* 6* 7* 8* 9* 10* 11* 12* 13*
Dias et al. (2016)
Nejatidan et al. (2015)
Frankenberger et al. (2008)
Kramer et al. (2008)
Otto & Schneider (2008)
Reiss (2006)
Schulte et al. (2005)
Smales & Etemadi (2004)
Schulz et al (2003)
Posselt & Kerschbaum (2003)
Hayashi et al (2000)
Fuzzi & Rappelli
Selection
Comparability
Outcome
Estatistics

B)

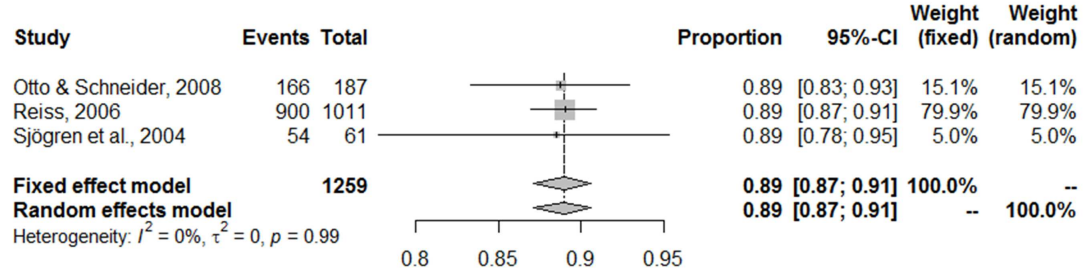

Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
0% 25% 50% 75% 100%
Low risk of bias
Unclear risk of bias
High risk of bias

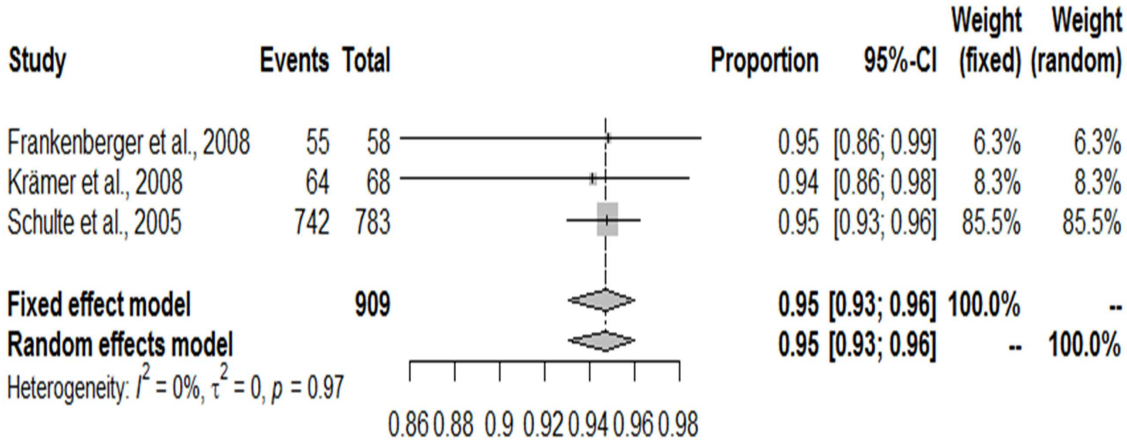

Sjögren et al.

A

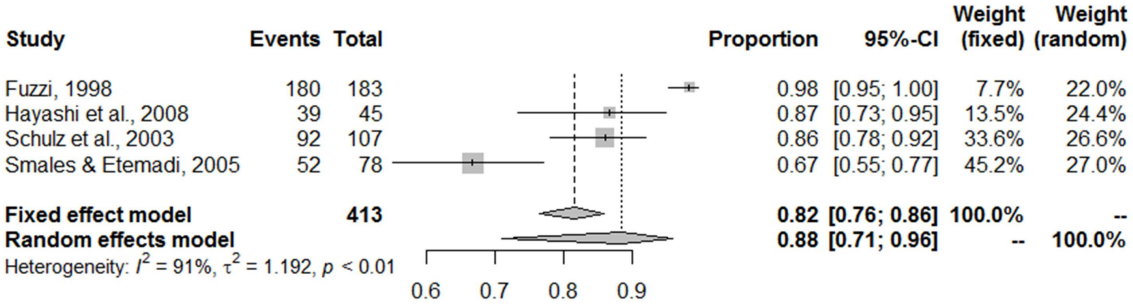

Study
Events Total
Proportion
95%-CI
Weight (fixed)
Weight (random)
Nejatidanesh et al., 2015 152 159 0.96 [0.91; 0.98] 6.6% 6.6%
Otto & Schneider, 2008 180 187 0.96 [0.92; 0.98] 6.6% 6.6%
Posselt & Kerschbaum, 2003 2270 2328 0.98 [0.97; 0.98] 55.5% 55.5%
Reiss, 2006 981 1011 0.97 [0.96; 0.98] 28.6% 28.6%
Sjögren et al., 2004 58 61 0.95 [0.86; 0.99] 2.8% 2.8%
Fixed effect model 3746 0.97 [0.97; 0.98] 100.0% --
Random effects model 0.97 [0.97; 0.98] -- 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.41
0.88 0.9 0.92 0.94 0.96 0.98

B

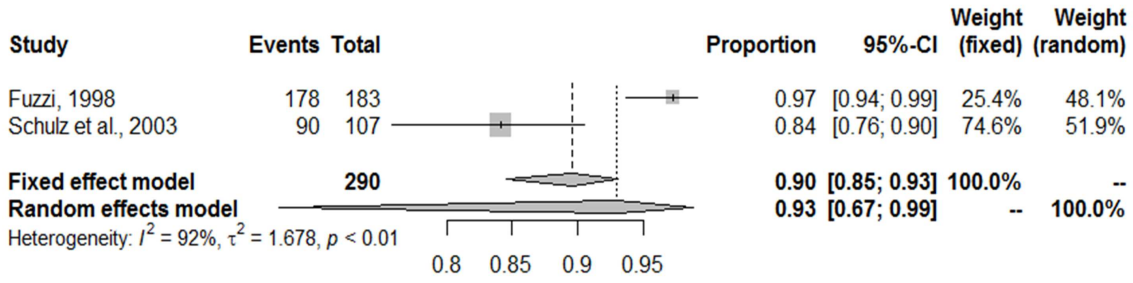

Study
Events Total
Proportion
95%-CI
Weight (fixed)
Weight (random)
Otto & Schneider, 2008 166 187 0.89 [0.83; 0.93] 15.1% 15.1%
Reiss, 2006 900 1011 0.89 [0.87; 0.91] 79.9% 79.9%
Sjögren et al., 2004 54 61 0.89 [0.78; 0.95] 5.0% 5.0%
Fixed effect model 1259 0.89 [0.87; 0.91] 100.0% --
Random effects model 0.89 [0.87; 0.91] -- 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.99
0.8 0.85 0.9 0.95


Study
Events Total
Proportion
95%-CI
Weight (fixed)
Weight (random)
Frankenberger et al., 2008 55 58 0.95 [0.86; 0.99] 6.3% 6.3%
Krämer et al., 2008 64 68 0.94 [0.86; 0.98] 8.3% 8.3%
Schulte et al., 2005 742 783 0.95 [0.93; 0.96] 85.5% 85.5%
Fixed effect model 909 0.95 [0.93; 0.96] 100.0% --
Random effects model 0.95 [0.93; 0.96] -- 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.97
0.86 0.88 0.9 0.92 0.94 0.96 0.98

A


Study
Events
Total
Proportion
95%-CI
Weight (fixed)
Weight (random)
Fuzzi, 1998 180 183 0.98 [0.95; 1.00] 7.7% 22.0%
Hayashi et al., 2008 39 45 0.87 [0.73; 0.95] 13.5% 24.4%
Schulz et al., 2003 92 107 0.86 [0.78; 0.92] 33.6% 26.6%
Smales & Etemadi, 2005 52 78 0.67 [0.55; 0.77] 45.2% 27.0%
Fixed effect model 413 0.82 [0.76; 0.86] 100.0% --
Random effects model 0.88 [0.71; 0.96] -- 100.0%
Heterogeneity: I^2 = 91%, τ^2 = 1.192, p < 0.01
0.6
0.7
0.8
0.9

B


Study
Events
Total
Proportion
95%-CI
Weight (fixed)
Weight (random)
Fuzzi, 1998 178 183 0.97 [0.94; 0.99] 25.4% 48.1%
Schulz et al., 2003 90 107 0.84 [0.76; 0.90] 74.6% 51.9%
Fixed effect model 290 0.90 [0.85; 0.93] 100.0% --
Random effects model 0.93 [0.67; 0.99] -- 100.0%
Heterogeneity: I^2 = 92%, τ^2 = 1.678, p < 0.01
0.8
0.85
0.9
0.95